REMARKS

Claims 67-79 are pending in the above-identified application. Claims 70-74 and 76-79 stand withdrawn from consideration as directed to a non-elected invention. Claims 67-69 and 75 are presently being examined.

Claim 67 has been amended herein to recite that the antimicrobial peptide is in isolated form. The amendment to claim 67 adds no new matter and Applicants respectfully request entry of the amendment.

Rejections under 35 U.S.C. § 101

The rejection of claim 67 under 35 U.S.C. § 101, for allegedly being directed to non-statutory subject matter respectfully is traversed. This rejection is rendered moot by the above-proposed amendment to claim 67, which as amended is directed to an isolated antimicrobial peptide. Accordingly, Applicants respectfully request removal of the rejection of claim 67, for allegedly being directed to non-statutory subject matter.

Rejections under 35 U.S.C. § 112, second paragraph

The rejection of claims 67-69 and 75 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention, respectfully is traversed. Applicants submit that claims 67-69 and 75 are clear and definite to one possessing the ordinary level of skill in the art in view of the specification.

Applicants again point out that the U.S. Court of Appeals for the Federal Circuit has indicated in its numerous decisions on the issue that definiteness of claim language must be analyzed, not in a vacuum, but in light of (1) the content of the particular application disclosure, (2) the teachings of the prior art, and (3) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. *See, e.g., In re Marosi*, 710 F.2d 799, 218 U.S.P.Q. 289 (Fed. Cir. 1983); *Rosemount, Inc. v. Beckman Instruments, Inc.*, 727 F.2d 1540, 221 U.S.P.Q. 1 (Fed. Cir. 1984); *W.L. Gore & Assocs., Inc. v.*

Garlock, Inc., 721 F.2d 1540, 220 U.S.P.Q. 303 (Fed. Cir. 1983); and *Atmel Corp. v. Information Storage Devices, Inc.*, 198 F.3d 1374, 53 U.S.P.Q.2d 1225 (Fed. Cir. 1999) (district court failed to consider the knowledge of one skilled in the art when interpreting the patent disclosure).

> The primary purpose of the definiteness requirement is to ensure that the claims are written in such a way that they give notice to the public of the extent of the legal protection afforded by the patent, so that interested members of the public, e.g., competitors of the patent owner, can determine whether or not they infringe. That determination requires a construction of the claims according to the familiar canons of claim construction.

All Dental Prodx, LLC v. Advantage Dental Prods., 309 F.3d 774, 779-80, 64 USPQ2d 1945, 1949 (Fed. Cir. 2002) (citations omitted).

The determination of whether a claim is invalid as indefinite "depends on whether those skilled in the art would understand the scope of the claim when the claim is read in light of the specification." *See N. Am. Vaccine, Inc. v. Am. Cyanamid Co.*, 7 F.3d 1571, 1579 (1993) (citation omitted).

With regard to the assertion that the phrase "mimetics thereof" is indefinite, Applicants respectfully submit that this term, viewed by the skilled person in light of the specification and what was known in the art, is sufficiently clear and definite to meet the requirements of paragraph 112.

According to the Federal Circuit, "[M]athematical precision is not required--only a reasonable degree of particularity and definiteness." *Exxon v. US*, 265 F.3d 1371, 1381; 60 U.S.P.Q.2d 1272, 1279 (Fed. Cir. 2001). Applicants submit that a reasonable degree of definiteness is provided to the skilled person viewing the phrase "mimetics therof" by teaching, for example, at page 42, lines 12-21, that the invention peptides can be conformationally stabilized by replacing selected amino acid in the original peptide with amino acids that restrict the motion of the peptide chain, for example, beta-branched, N-methyl, alpha,beta-dehydro, alpha,alpha-dialkyl and D-amino acids. The specification also teaches that substitutions of D- or other unusual amino acids into the peptide templates can extend the half-life of an invention

peptide. The skilled person would have understood with clarity that mimetics include peptidomimetics, peptoids, or other peptide-like polymers as well as non-polymeric compounds upon which functional groups that mimic a peptide are positioned.

Another significant issue with regard to clarity is the knowledge of one skilled in the art when interpreting the patent disclosure. Notably, the Federal Circuit has overturned cases on the indefiniteness issue where the knowledge of one skilled in the art was not taken into account. *See Atmel Corp. v. Information Storage Devices, Inc.*, 198 F.3d 1374, 53 U.S.P.Q.2d 1225 (Fed. Cir. 1999). With regard to the art-knowledge, the manufacture of peptidomimetics was well known in the art. As evidence that peptidomimetics were well known in the art at the time the invention was made, Applicants submit herewith as Exhibit A an excerpt from Goodman and Ro, *Peptidomimetics for Drug Design*, in "Burger's Medicinal Chemistry and Drug Discovery" Vol. 1 (ed. M.E. Wolff; John Wiley & Sons 1995), pages 803-861. Goodman and Ro describe representative types of peptidomimetics routinely prepared in the art including peptidomimetics that incorporate non-naturally occurring amino acids, peptidomimetics having modified linkages between consecutive residues, peptidomimetics in which a peptide bond is replaced with amide isoteres, and transformations of secondary structure of peptides to nonpeptidic molecules. Goodman and Ro indicate that peptidomimetics can be prepared that have advantages over the corresponding native peptide:

> It is widely believed that such modifications will enhance the desirable properties and avoid undesirable properties of native peptides. Many analogs incorporating mimetic components have exhibited improved pharmacological and pharmakinetic properties, including increased bioactivity, selectivity, metabolic stability, absorption and lower toxicity. Some of these mimetic analogs are currently used as therapeutic agents.

Page 805, left column, first partial paragraph.

With regard to mimetics that incorporate one or more D-amino acids, which are disclosed in the specification at page 42, lines 12-21, Goodman and Ro indicate:

> The incorporation of D-amino acids would be one of the most popular modifications. In naturally occurring peptides, D-amino acids are often observed as a critical residue for bioactivity.... In many cases, incorporation of a D-amino acid increases bioactivities of peptides including enkephalins, somatostatin and oxytocin. When the second residue of enkephalin (Gly) was replaced with DALA, the resulting analog showed a higher bioactivity and metabolic stability than the parent.

[Citations omitted]

Page 833, left column, first full paragraph.

Thus, this reference corroborates that incorporation of D-amino acids was well known in the art. In conclusion, Goodman and Ro offer the following observation regarding the state of the current art of peptidomimetic design:

> It is clear that peptidomimetics and nonpeptidic analogs represent the present and future in drug design. Hopefully, this chapter has provided insight into the chemistry currently used to explore and design novel drug structures. [Emphasis added]

Page 848, right column, final paragraph.

In view of the above, Applicants respectfully submit that the term "mimetics" was well known in the art at the time the subject application was filed such that the skilled person would understand the scope of claim 67 when the claim is read in light of the specification.

As further evidence that undue experimentation would not have been required to prepare a mimetic of a antimicrobial parent peptide that retains the antimicrobial activity of the parent peptide, Applicants submit herewith as Exhibit B as publication by Cody et al., *J. Med. Chem.* 40:2228-2240 (1997), which describes design and preparation of the Endothelin-A/Endothelin-B receptor antagonist PD156252 (page 2228, abstract). Cody et al. report preparation of the PD156252 peptidomimetic of the C-terminal hexapeptide of endothelin by substitution of a

single non-natural amino acid and N-methylation of the amide bond connecting two of the amino acid residues of the parent hexapeptide (page 2234, right column, second paragraph). As reported in Cody et al., the substitution of a non-natural amino acid into the parent endothelin C-terminal hexapeptide resulted in a highly potent ETA/ETB receptor antagonist, and subsequent N-methylation of the amide bond between the isoleucine residues 19 and 20 further conferred enhanced stability on the peptidomimetic (page 2234 to page 2235, right column, "Conclusions"). Thus, these results corroborate that the skilled artisan reading the specification would understand the scope of claim 67 with sufficient clarity as encompassing, for example, a non-natural amino acid or N-methylated amide bond incorporated into an antimicrobial peptide of the invention.

In sum, Applicants respectfully submit that those skilled in the art would understand the scope of claims 67-69 and 75 when the claims are read in light of the specification. In view of the above remarks and exhibits, Applicants respectfully request that the Examiner remove the rejection of claims 67-69 and 75 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Rejections under 35 U.S.C. § 102

Applicants respectfully traverse the rejection of claims 67-69 and 75 under 35 U.S.C. § 102(b), as allegedly anticipated by United States Patent No. 5,409,898, to Darveau et al. The Office Action alleges that, since the claim does not define the "mimetics thereof," any substituted peptide that retains antimicrobial activity would fall within the scope of the claim (current Office Action, Paper No. 23, page 4, section 3).

Applicants respectfully disagree that the peptides set forth in the '898 patent, which differ from the claimed antimicrobial peptides by having non-identical natural amino acid residues at several positions qualify as mimetics of the claimed peptides. Mimetics are "chemical structures derived from bioactive peptides which imitate natural molecules." Goodman and Ro, *supra*, sentence bridging pages 804 and 805). A natural peptide having non-identical natural amino

acid residues at several positions compared to the claimed antimicrobial peptide does not represent a mimetic of an antimicrobial peptide of claims 67-69 and 75.

Accordingly, removal of the rejection of claims 67-69 and 75 under 35 U.S.C. § 102(b), as allegedly anticipated by United States Patent No. 5,409,898, to Darveau et al. respectfully is requested.

Applicants respectfully traverse the rejection of claims 67-69 and 75 under 35 U.S.C. § 102(b), as allegedly anticipated by Kupsch et al., *EMBO J.*, 12(2): 641-650 (1993). The Office Action alleges that claims 67 and 68 are anticipated by the description in Kupsch et al. of a member of the variable opacity (Opa) outer membrane family of proteins that is designated OPA 65 and has 236 amino acids, including the core sequence ARYRKWK.

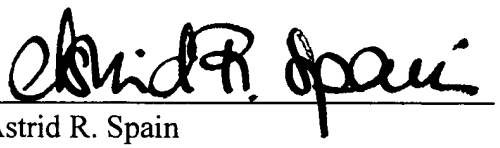
Base claim 67 discloses an isolated antimicrobial peptide having 13 to 74 amino acids. The Opa 65 peptide has 236 amino acids as pointed out in the current Office Action. Accordingly, the Opa 65 peptide does not fall within the scope of claim 67 and cannot anticipate either base claim 67 or dependent claim 68. Accordingly, Applicants respectfully request removal of the rejection of claims 67and 68 under 35 U.S.C. § 102(b), as allegedly anticipated by Kupsch et al., *EMBO J.*, 12(2): 641-650 (1993).

CONCLUSION

In light of the Amendments and Remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. Should the Examiner have any questions, he/she is invited to call the undersigned attorney.

Respectfully submitted,

November 21, 2003
Date



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